REMARKS

Claims 1-75 remain under active prosecution in the present application. Applicants respectfully assert that all amendments are supported by the original disclosure and do not introduce new matter. Moreover, Applicants further respectfully assert that the amendments merely clarify the scope of the claims.

In the subject Office Action dated July 14, 2006, applicant's appreciate Examiner's clarification that the elected invention will include claim 39, on top of claims 40 and 42.

Claims 1-38, 41, and 43-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 39-40 and 42 are examined in the instant application. Claims 39 and 40 have now been amended.

Double Patenting

The Examiner has rejected claims 39, 40 and 42 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, and 8 of U.S. Patent No. 6,838,428 B2. Although the conflicting claims are not identical, the Examiner contends that they are not patentably distinct from each other because the instant claims are similar to said patented claims.

Upon disposition of all matters related to patentability in the present application, Applicants will file a terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) on an expedited basis to overcome an actual or provisional rejection based on a nonstatutory double patenting grounds that are present in the final claims.

Claim Rejections - 35 USC §112

The Examiner has rejected claims 39, 40 and 42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Examiner contends that the claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 39, 40, and 42 are drawn to a method of treating pulmonary disease in a subject comprising the administration to a subject in need of such treatment a therapeutically effective amount of a formulation comprising a SP-C therapeutic, wherein said therapeutic is a SP-C protein.

The Examiner contends that the breadth of the claims encompasses treating any subject with any amount of an isolated SP-C protein, which the Examiner contends reads on protein therapy.

Applicants respectfully traverse this rejection. The rejection based on the several reviews, *e.g.*, Brown (2005, *Expert Opinion Drug Delivery*, Vol. 2(1), pgs. 29-42), cited by the Examiner is based upon the alleged unpredictability in "protein therapy" and recombinant SP-C. Applicants respectfully assert that the Examiner misunderstands the therapy involved with the present invention with either SP-C or SP-D.

Neither therapy of the present invention is intended to deliver proteins systemically, but to deliver them to the surface of the airways and alveoli. Various readily available and well-known delivery methods such as aerosol or instillation therapy have been used for a wide variety of disorders and is *standard* in clinical practice. Numerous drugs have been delivered to the airway epithelium (*e.g.* glucocorticoids for treatment of asthma and surfactant therapy for acute respiratory distress syndrome). In the latter, protein-lipid mixtures are administered to the lung, where the effects of the drug are local. The surfactant proteins function in the airways and in the surface epithelium, and can be readily delivered for therapy of lung disease.

In the attached Declarations and supplemental Information Disclosure Statement, Applicants have submitted several references demonstrating the feasibility of this therapy with SP-D and SP-B for acute diseases as tested in mice or sheep (see, for example, Hokuto et al., J. Clin. Invest. 113:28-37, 2004; Ikegami et al., Am. J. Physiol. 288:L552-L561, 2005; and Ikegami et al., Am. J. Respir. Crit. Care Med. 173:1342-1347, 2006). Therapy with SP-B, SP-C, and SP-D has been highly effective in rodent and sheep models of acute lung disease, and there is no reason to expect that they cannot be delivered chronically by aerosol or instillation. The present invention provides for the treatment for SP-C

abnormalities and such treatment is intended to be local. Applicants have now amended the claims to clarify such local delivery.

The references now provided by the Applicants herein use both recombinant SP-C-like peptides, recombinant SP-D, and purified SP-B as examples for therapy of acute lung disorders. Patients with mutations in the SP-C gene generally do not produce the active peptide (SP- C) needed in the airway. Even when the mutation is heterozygous, processing of the normal preproprotein (proSP-C) to active SP-C is inhibited by the mutant protein. Thus, replacement of the SP-C peptide to the lung represents a potential therapy.

Applicants have shown that deficiency of SP-C *per se* also causes severe lung disease in the knockout mice and have identified human patients that lack expression of both proSP-C and SP-C; therefore replacement of SP-C represents a potential therapy for this rare subset of patients when given into the lung. Finally, clinical mutations in which proSP-C is misprocessed or its synthesis is inhibited secondarily, as in severe lung injury, will have a decreased SP-C that can be replaced by delivery of the recombinant protein to the lung. Applicants have also shown that in conditions in which a surfactant protein is deficient, but not absent, additional surfactant protein can prevent further lung injury (*e.g.* as shown in Hokuto et al., J. Clin. Invest. 113:28-37, 2004).

Applicants assert that to make use of the present invention, one would generally produce a formulation of the surfactant protein, recombinant SP-C or SP-C-like peptide, with or without lipid carriers, for example and without limiting ourselves in any way, mixed 1-5% by weight with phosphytidalcholine (30-50 mg/kg), suspended in normal saline or buffered saline and given intratracheally or by aerosol. The protein-lipid mixture can be administered by aerosol or instillation to the airway surface. Since the half-life of surfactant components, including lipids and proteins is 6-12 hours in the mature lung, therapy could be repeated Q12h to daily. Such preparations are utilized routinely for the surfactant therapy of acute respiratory distress syndrome in premature infants. These infants have been successfully treated for many years in clinical practice. References given are standard for delivery of protein to the lung, and are not intended for systemic delivery of

the peptide. Surfactant therapy for acute lung disease (RDS) in preterm infants, providing a lipid or lipid-protein mixture to the lung has been a standard therapy for RDS in preterm infants for more than 25 years (see, for example Whitsett, J.A.: Pulmonary surfactant and respiratory distress syndrome in the newborn infant. In: The Lung: Scientific Foundations, 2nd Edition, R.G. Crystal, J.B. West, E.R. Weibel and P.J. Barnes (*eds.*). Raven Press, New York, NY, Chapter 165:2167-2177, 1996).

In view of the submitted Declarations, cited references and the claim amendments, Applicants submit that a skilled artisan would have sufficient guidance in the instant disclosure to make and use the full scope of the claimed embodiment. One of normal skill in the art would be able to rely on the state of the art of *in vivo* protein therapy to practice the claimed method in view of the disclosure regarding a method of treatment in the instant specification.

Thus, Applicants respectfully request that the rejections based on 35 USC 112 be withdrawn.

Claim Rejections - 35 USC § 102

The Examiner has rejected claims 39-40, and 42 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,838,428 B2

The Applicants have provided a showing under 37 CFR 1.132 in the enclosed Declarations that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another".

Therefore, Applicants ask that the rejection under 35 U.S.C. 102(e) be withdrawn.

CONCLUSION

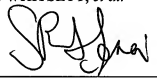
In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage

the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com.

The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

JEFFREY A. WHITSETT, *et al.*

By 

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